

**FIG.\_1****FIG.\_1A****FIG.\_1B****FIG.\_1A****SEQ ID NO: 1****Nucleotide Sequence Tankyrase Homologue isotype1**

CTTTGAAGACACTGGATTTTCATACTTTTGCCTGGGGTTATCTCTCTGTGTCTCACTACATAGACAAATA  
TTAGCTGTGAGCAGATCTTTTTTTGTTGCTTCTTGTAGTCCCCAGTTTAGCAGAAACATTCTGTGAGA  
TAGATGTGGGAAAGGAATTCTAGCAAGAGTTTTGTCACTGTATCATAAGGTTGTGATTTACATATTTAA  
GTTTTATACTTTGAACATCTGAAAATGTATACATACTAAATATGCAGAACTCTATTGTAGAGTGAGAAA  
CATTTGAACTTTGAGCTTTCAGTCACTTATTTTGTATTCTTTCTTTGAGGTTAGCAGTAGTACCACCCA  
AGGCACTGCTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAAGGTTTTGGGCG  
GAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAGTGTCCAAGCACGTGATGATGGGGGCCTTAT  
TCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCCTTTTGCGACATGGTGCAGA  
CCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAATTAAAGGAAAGATTGATGT  
TTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAGATGGAAGGACAGCATTGGA  
TTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGC  
CAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAATGTCAACTGCCACGCAAGTGA  
TGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTACAGCTGTTACT  
GCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCATTACACAATGCCTGTTCTTA  
TGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAAATGCAATGGACTTGTGGCA  
ATTCACCTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTTCTCTTCTTAAAGTTATGG  
TGCAGACCCAACTGCTCAATTGTCACAATAAAGTGCTATAGACTTGGCTCCCACACCACAGTTAAA  
AGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCG  
AATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAAACACATGAAACAGCATTGCA  
TTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACTGTTGCTAAGAAAAGGAGCAAA  
CATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTGAGAAAGCTCATAATGATGT  
TGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACA

CAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCTATGGGTGTGATCCTAACAT  
TATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGG  
TATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTGAAAC  
TGTAaaaaaactGTGTACTGTTCAAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCACT  
TCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAAATATCTGCTACAGCATGGAGCTGATGTGCA  
TGCTAAAGATAAAGGAGGCCTTGTACCTTTGCACAATGCATGTTCTTATGGACATTATGAAGTTGCAGA  
ACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAATTTACACCTTTACATGAAGC  
AGCAGCAAAAGGAAAATATGAAATTTGCAAACCTTCTGCTCCAGCATGGTGCAGACCCTACCAAAAAAA  
CAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATATTCAAGATCTGCTTAGGGG  
AGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGAAGAAGTTGTCTTCTCCTGA  
TAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATTTAGCAGCTGGTTATAATAA  
TTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCCAAGACAAAGGAGGACTTAT  
TCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTACTAATAAAGTATAATGCATG  
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TTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGA  
TTTAGTTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCCTCTTG  
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ATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACTTATCTGGGAGTTTTTCAGAACTGTC  
TTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAAGGAGGTTCCAGGAGTAGA  
TTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGGATATATTTGAGAGAGAACA  
GATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGG  
ACATAGGCACAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTTAACCCATATTT  
AACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTGATGATAAAGAGTTTCAGTC  
TGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCATGCAGGTGGAATCTTCAA  
CAGATACAATATTCTCAAGATTGAGAAGTTTGTAAACAAGAACTATGGGAAAGATACACTCACCGGAG  
AAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTATTTTCATGGGTCTCCTTTTGT  
GAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCAT  
TTATTTTGTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTAAGGTGTTCC  
AGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTTGCCGGGTAACCTTGGGAAA  
GTCTTTTCTGCAAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCATCACTCAGTCACTGGTAG  
GCCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAGAACAGGCTTATCCTGAGTA  
TTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAATAGTTATTTTAAGAACTA  
ATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAAAA  
AA

**FIG. 1B**

**FIG.\_2****FIG.\_2A****FIG.\_2B****FIG.\_2A****SEQ ID NO: 2****Nucleotide Sequence Tankyrase Homologue isotype2**

CGCGCTGCTCCGCCCCGCGCGGGGCAGCCGGGGGGCAGGGAGCCCAGCGAGGGGCGCGCTGGGCGCGG  
CCCATGGGACTGCGCCGGATCCGGTGACAGCAGGGAGCCAAGCGGCCCCGGGCCCTGAGCGCGTCTTCTC  
CGGGGGGCGCTCGCCCTCCTGCTCGCGGGGCGGGGCTCCTGCTCCGGTTGCTGGCGCTGTTGCTGGCTG  
TGGCGGCGGCCAGGATCATGTGCGGTGCGCGCTGCGCCGGCGGGGAGCGGCCTGCGCGAGCGCCGCGG  
CCGAGGCCGTGGAGCCGGCCGCCGAGAGCTGTTGAGGCGTGCCGCAACGGGGACGTGGAACGAGTCA  
AGAGGCTGGTGACGCCTGAGAAGGTGAACAGCCGCGACACGGCGGGCAGGAAATCCACCCGCTGCACT  
TCGCCGCAGGTTTTGGGCGGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCAC  
GTGATGATGGGGGCGCTTATTCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC  
TTTTGCGACATGGTGCAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAA  
TTAAAGGAAAGATTGATGTTTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAG  
ATGGAAGGACAGCATTGGATTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAG  
ATGAACTCTTAGAAAGTGCCAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATG  
TCAACTGCCACGCAAGTGATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAA  
AGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCAT  
TACACAATGCCTGTTCTTATGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAA  
ATGCAATGGACTTGTGGCAATTCCTCCTCTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTT  
CTCTTCTCTTAAGTTATGGTGCAGACCCAACACTGCTCAATTGTGACAATAAAAGTGCTATAGACTTGG  
CTCCACACCACAGTTAAAGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCAC  
GAGAAGCTGATGTTACTCGAATCAAAAAACATCTCTCTGGAATGGTGAATTTCAAGCATCCTCAAA  
CACATGAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACTGT  
TGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTG  
AGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAACATGAAGCAAAGGTTAATGCTCTGGATAATC

TTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCT  
ATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAATGTAC  
AGCAACTCCTCCAAGAGGGTATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAA  
AGGCTGGAGATGTCGAAACTGTAAAAAACTGTGTACTGTTTCAGAGTGTCAACTGCAGAGACATTGAAG  
GGCGTCAGTCTACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAAATATCTGCTAC  
AGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCTTGTACCTTTGCACAATGCATGTTCTTATG  
GACATTATGAAGTTGCAGAACTTCTTGTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAAT  
TTACACCTTTACATGAAGCAGCAGCAAAAGGAAAATATGAAATTTGCAAACTTCTGCTCCAGCATGGTG  
CAGACCCTACCAAAAAAACAGGGATGGAAATACTCCTTTGGATCTTGTAAAGATGGAGATACAGATA  
TTCAAGATCTGCTTAGGGGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGA  
AGAAGTTGTCTTCTCCTGATAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATT  
TAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCC  
AAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTAC  
TAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTCACACCTTTGCACGAAGCAGCCC  
AAAAGGGACGAACACAGCTTTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGG  
AAGGACAAACACCTTTAGATTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCC  
CATCTGCTCTGCCCTCTTGTTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAG  
ATGCTCTCTCTTCAGGTCCATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACTTATCTG  
GGAGTTTTTTCAGAACTGTCTTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCAGTTTGGAGAAAA  
AGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGG  
ATATATTTGAGAGAGAACAGATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGA  
TTGGAATCAATGCTTATGGACATAGGCACAACTAATTAAGGAGTCGAGAGACTTATCTCCGGACAAC  
AAGGTCTTAACCCATATTTAACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTG  
ATGATAAAGAGTTTCAGTCTGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTC  
ATGCAGGTGGAATCTTCAACAGATACAATATTCTCAAGATTGAGAAGGTTTGTAAACAAGAACTATGGG  
AAAGATACACTCACCGGAGAAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTAT  
TTCATGGGTCTCCTTTTGTGAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTG  
GTATGTTTGGAGCTGGCATTATTTTGTGCTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTG  
GAGGAGGTACTGGGTGTCCAGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTT  
GCCGGGTAACCTTGGGAAAGTCTTTCCTGCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTC  
ATCACTCAGTCACTGGTAGGCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAG  
AACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTTCGATGGATAAA  
TAGTTATTTTAAGAACTAATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTAC  
TCCTTTGCTGAAAAAAAAAAAA

**FIG.\_2B**

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**SEQ ID NO: 3****Amino Acid Sequence Tankyrase Homologue isotype1**

GFGRKDVVEYLLQNGASVQARDDGGLIPLHNACSFSGHADEVNLLLRHGADPNARDNWNYPPLHEAAIKG  
KIDVCIVLLQHGAEP TIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNVNC  
HASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVT ELLVKHGACV NAM  
DLWQFTPLHEAASKNRVEVCSLLSYGADPTLLNCHNKSAIDLAPTQPKERLAYEFKGHSL LQAAREA  
DVTRIKKHL SLEMVNFKHPQTHETALHCAAASPYPKRKQICELL LRKGANINEKTKEFLTPLHVASEKA  
HNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGHLQTCRLLSYGCDPNII SLQGFTALQMGNE NVQQL  
LQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHG  
ADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVVNVADLWKFTPLHEAAAKGKYEICKLLLQHGADP  
TKKNRDGNTPLDLVKDGD TDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHLAA  
GYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQKG  
RTQLCALLLAHGADPTLKNQEGQTPDLV SADDVSALLTAAMPPSALPSCYKPQVLNGVRS PGATADAL  
SSGPSSPSSLSAASSLDNLSGSFSELSSVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMDIF  
EREQITLDVLVEMGHKELKEIGINAYGHRHKL IKGVERLISGQQGLNPYLT LNTSGSGTILIDLSPDDK  
EFQSVEEEMQSTVREHRDGGHAGGIFNRYN ILKIQVCNKKLWERYTHRRKEVSEENHNHANERMLFHG  
SPFVNAI IHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYIGGGTGCPVHKDRSCYI CHRQLLFCRV  
TLGKSFLQFSAMKMAHSPPGHHSVTGRPSV

**FIG.\_3**

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SEQ ID NO: 4

**Amino Acid Sequence Tankyrase Homologue isotype2**

RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQAARALSASSPGGLALLLAGPGLLLRLLALLLAV  
AAARIMSGRRRCAGGGAACASAAAEAVEPAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHF  
AAGFGRKDVVEYLLQNGANVQARDDGGLIPLHNACSFQHADEVNLLLRHGADPNARDNWNYPPLHEAAI  
KGKIDVCIVLLQHGAEPTIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV  
NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTPELLVKHGACVN  
AMDWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSALDLAPTQPKERLAYEFKGHSLQAAAR  
EADVTRIKKHLSELMVNFKHPQTHETALHCAAASPYPKRKQICELLRKGANINEKTKEFLTPLHVASE  
KAHNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGLHQTCLLLSYGCDPNIISLQGF TALQMGNEVQ  
QLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQ  
HGADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVVNVADLWKFTPLHEAAAKGKYEICKLLLQHGA  
DPTKKNRDGNTPDLVKGDTDIQDLLRGDAALLDAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHL  
AAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQ  
KGRTQLCALLLAHGADPTLKNQEGQTPDLVVSADDVSALLTAAMPPSALPSCYKPQVLNGVRSFGATAD  
ALSSGPSSPSSLSAASSLDNLSGSFSELSSVSSSGTEGASSLEKKEVPGVDFSIQFVRNLGLEHLMD  
IFEREQITLDVLVEMGHKELKEIGINAYGHRHKLKIGVERLISGQGLNPLYTLNTSGSGTILIDLSPD  
DKEFQSVVEEMQSTVREHRDGGHAGGIFNRYNLIKIQVCNKKLWERYTHRRKEVSEENHNHANERMLF  
HGSPFVNAIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFC  
RVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

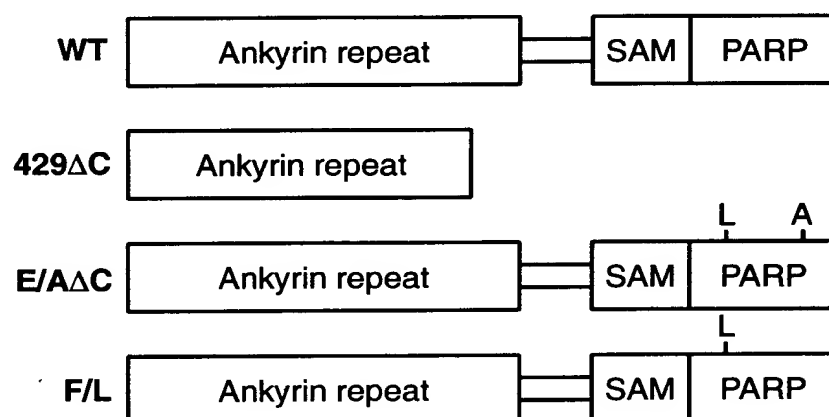
**FIG. 4**

### Schematic Presentation of Dominant Negative Mutants for Tankyrase Homologue

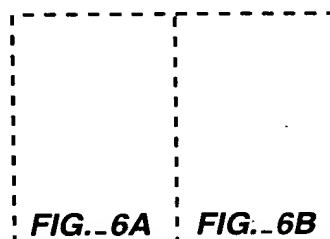
#### Dominant Negative Mutants

Truncation: 429 $\Delta$ C- of the C-terminal catalytic domain – truncation of the catalytic domain of PARP acts as a dominant negative when overexpressed *in vivo* (Oncogene 1999 Nov 25; 18(50):7010-5)

Point mutant: E945A $\Delta$ C- conserved residue in PARP domain, thought to be important in NAD<sup>+</sup> binding



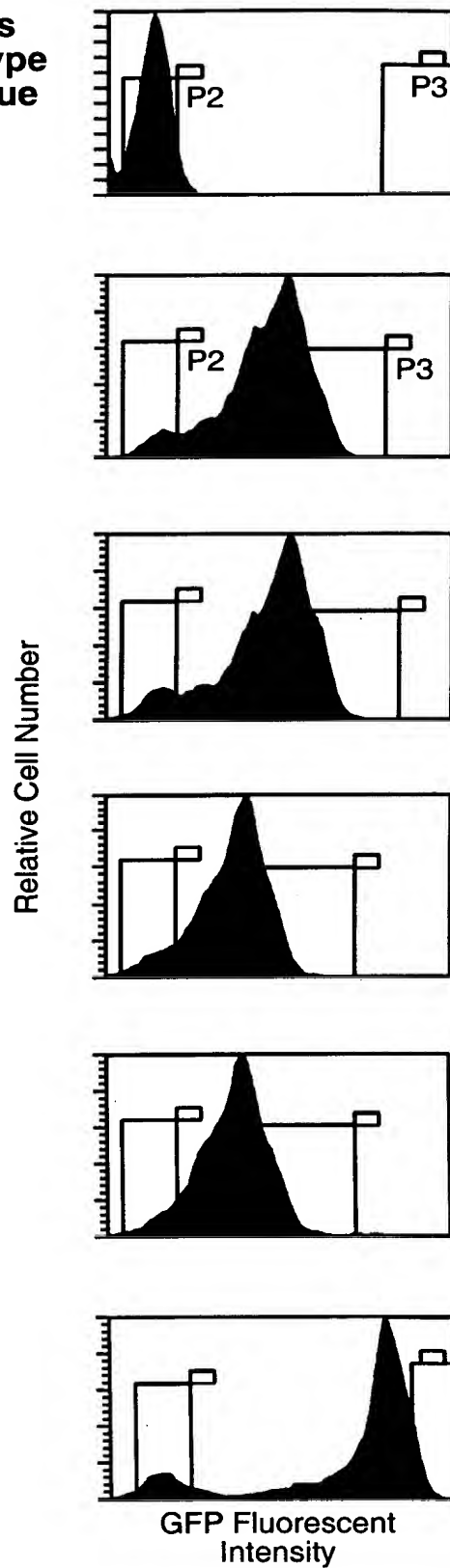
**FIG.\_5**



**FIG.\_6**

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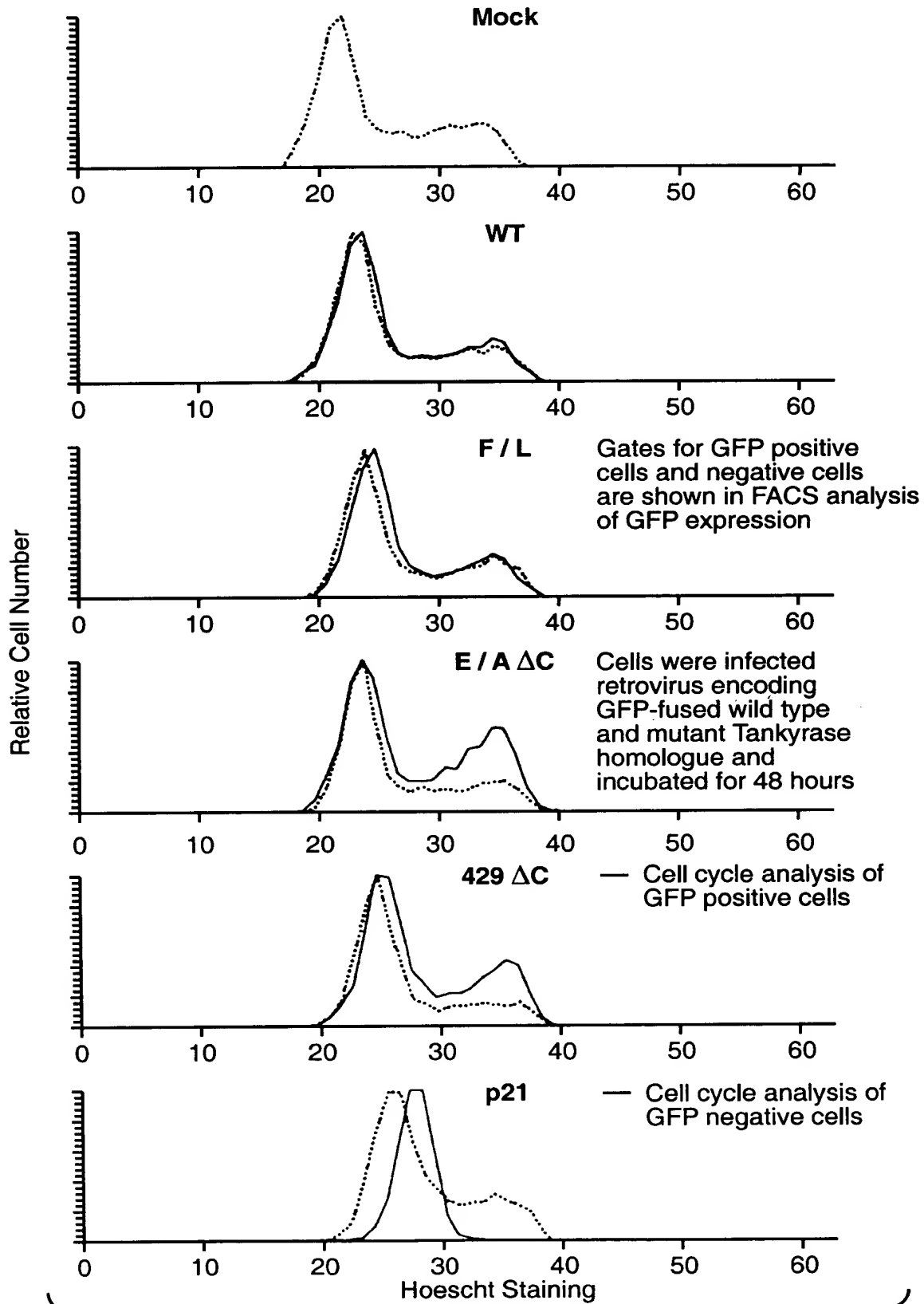
**Cell Cycle Analysis of A549 Cells  
Infected With GFP-fused Wild Type  
and Mutant Tankyrase Homologue**



**FIG. 6A**

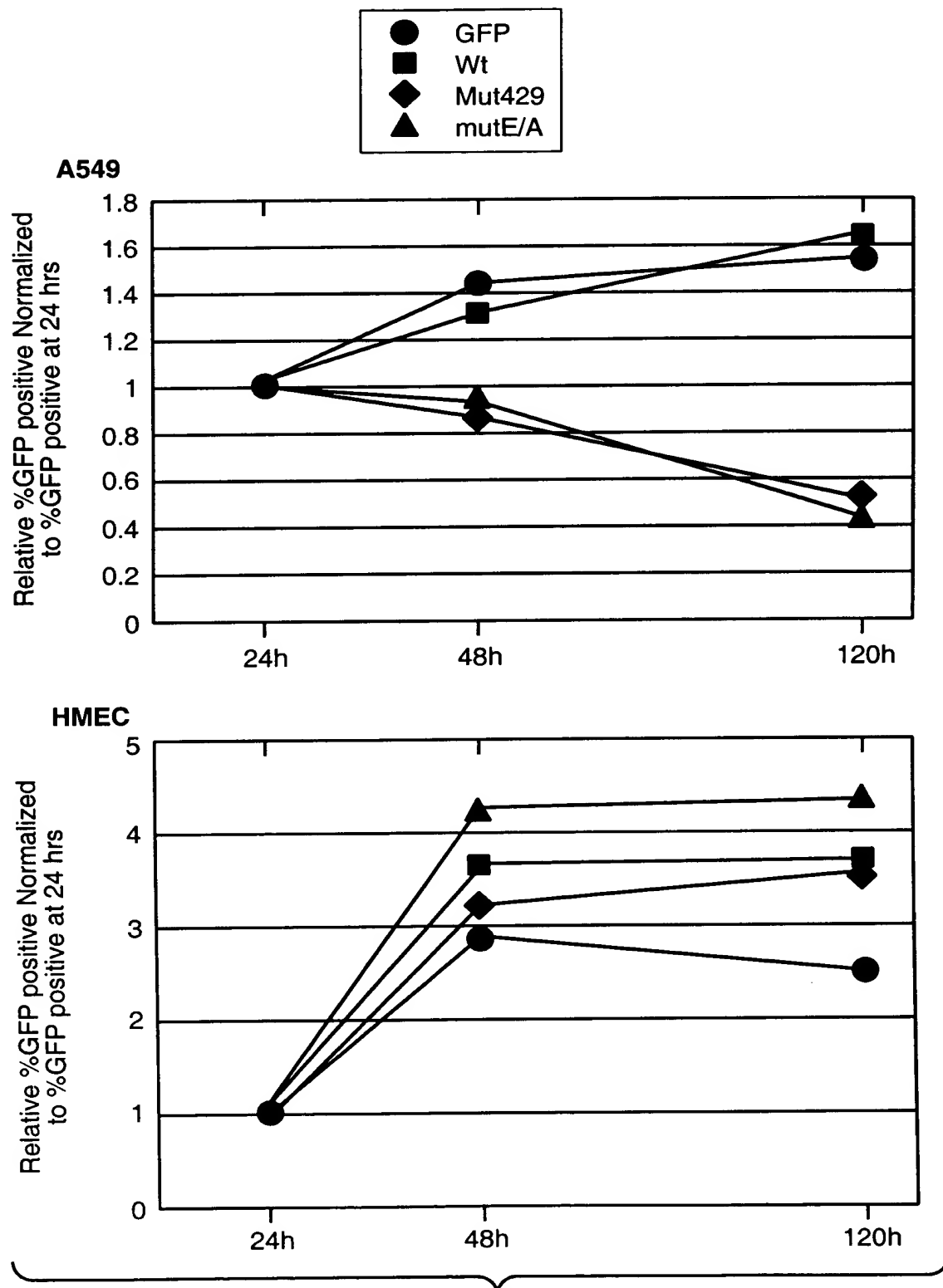


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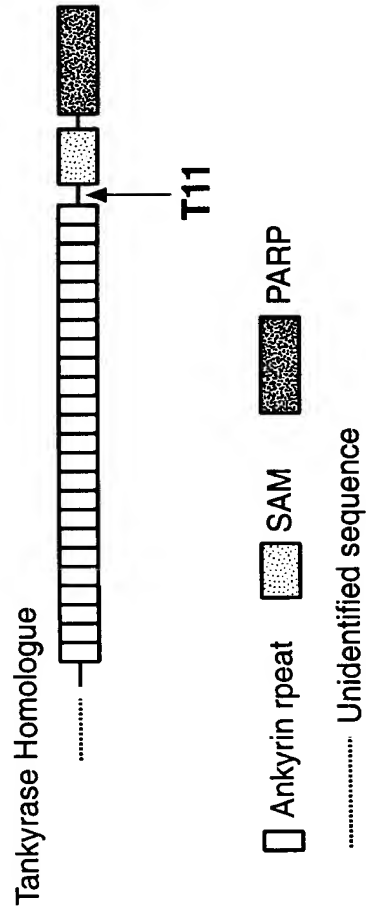
**FIG. 6B**

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**Kinetics of GFP Positive cells in A549 Cells and Human  
Mammary Epithelial Cells (HMEC) After Retrovirus Infection  
Encoding GFP-fused Wild Type and Mutant Tankyrase Homologue**

**FIG. 7**

# The Binding Site of Antisense Oligos Against Tankyrase Homologue





## T11

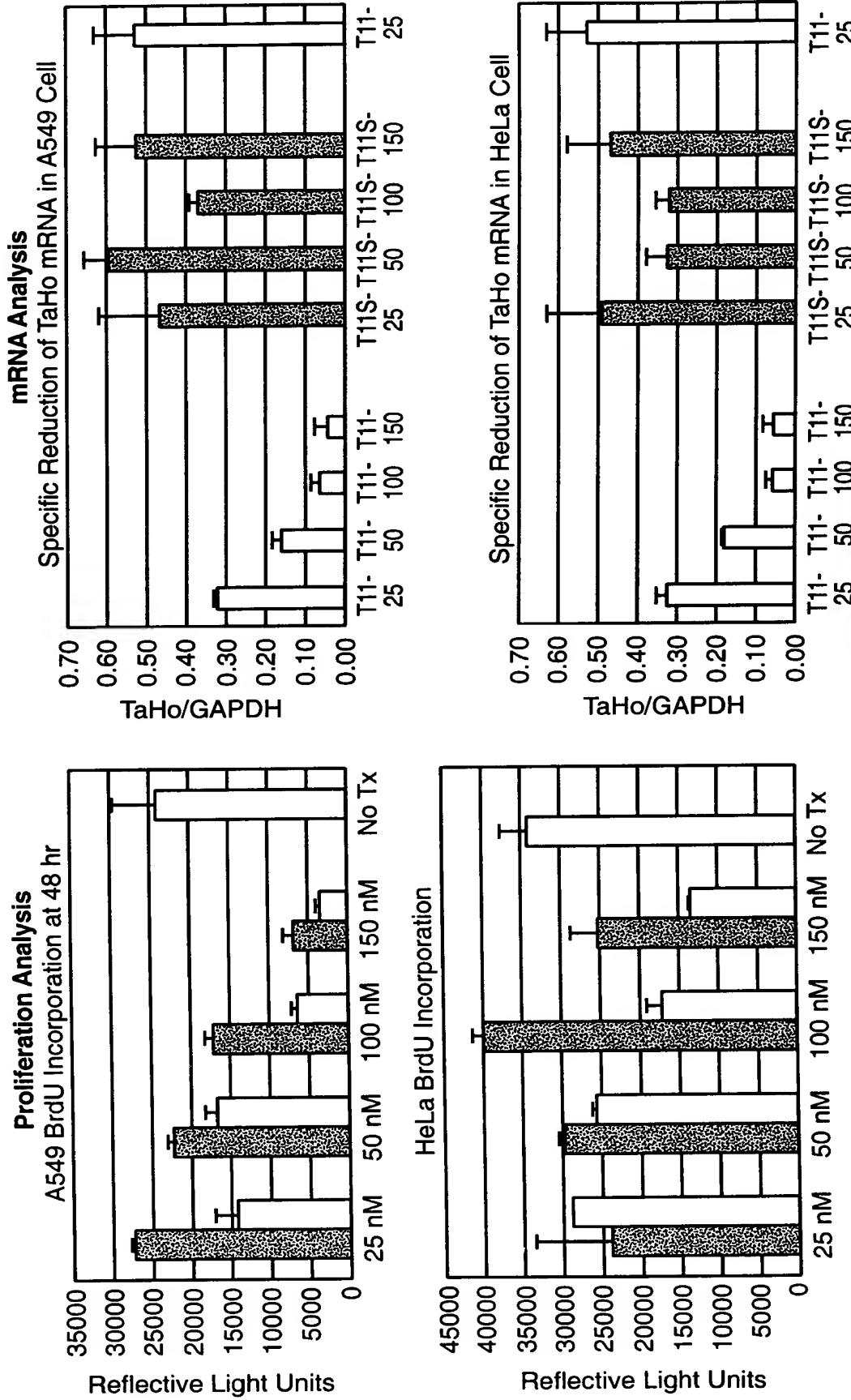
	GTGGAACACAGAGGGTGCTTCC	
Tankyrase Homologue	GTGGAACACAGAGGGTGCTTCCAGTTTGGAGAAAAAGGAGGTTCCAGGAGTAGATTTTAGCAT	2838
Tankyrase	ATGCAGGGGATGGCGCCGCGGGAACAGAAAAGGAAGGAGAAAGTTGCTGGTCTTTGACAT	3091
	** *	

FIG.\_8

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# **Anti-Proliferative Phenotype of Antisense Oligonucleotides Against Tankyrase Homologue in A549 and HeLa Cells**

 T11-SCR  
 T11

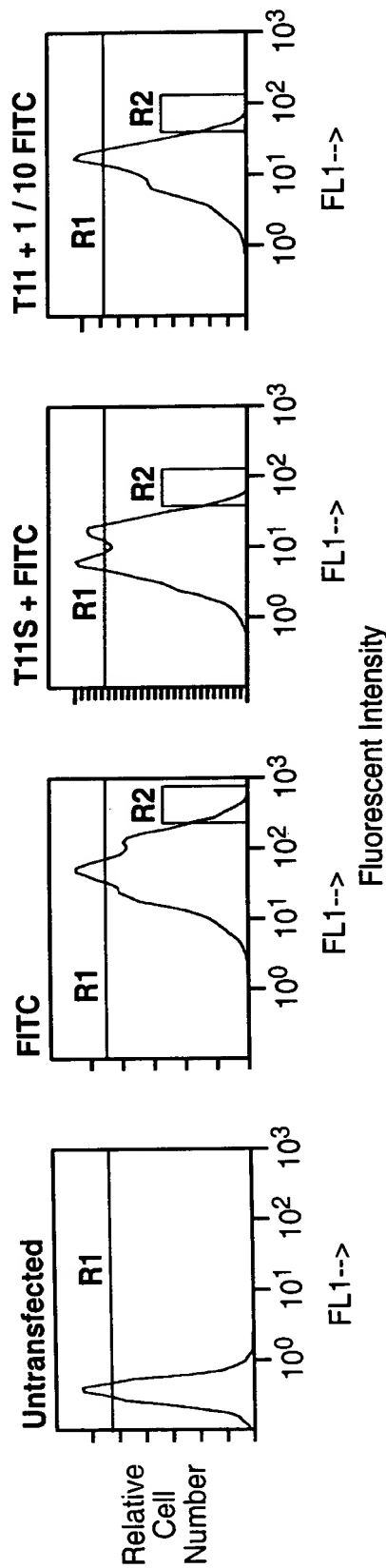


**FIG.\_9**

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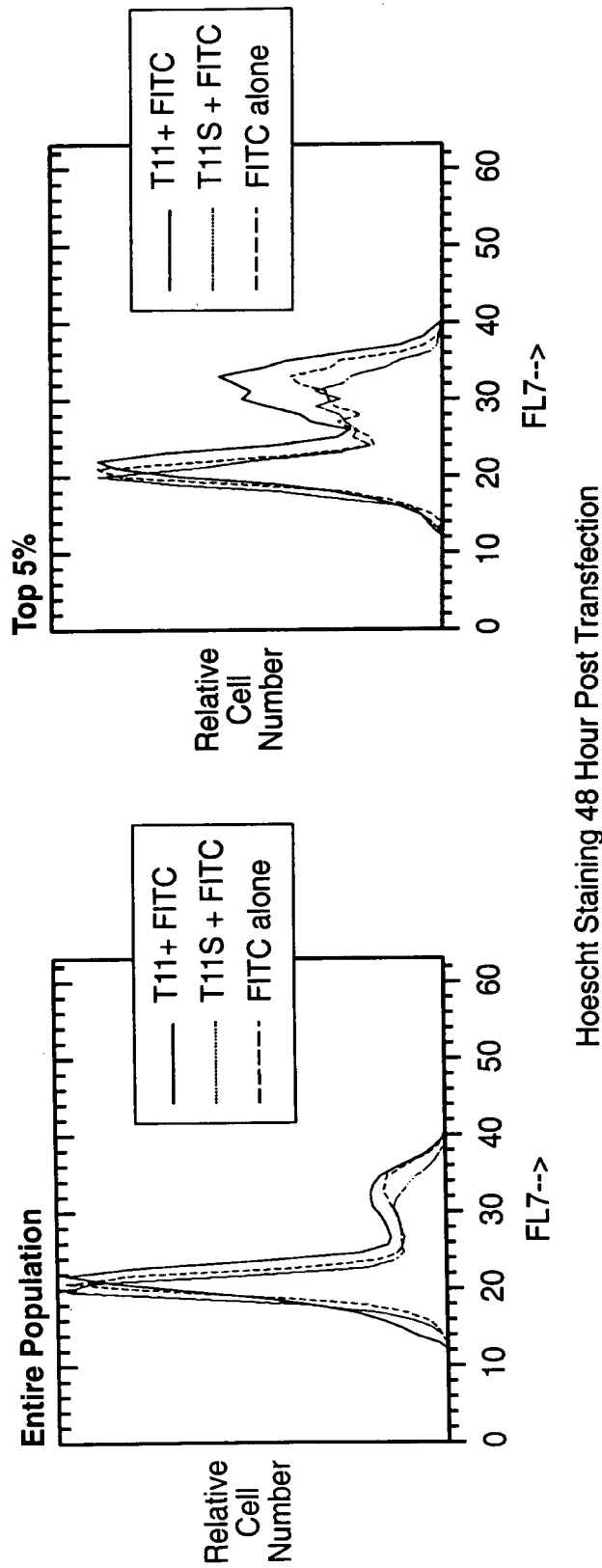
Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC), After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle

Gates for Cell Cycle Analysis

**FIG.. 10A**

Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC), After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle

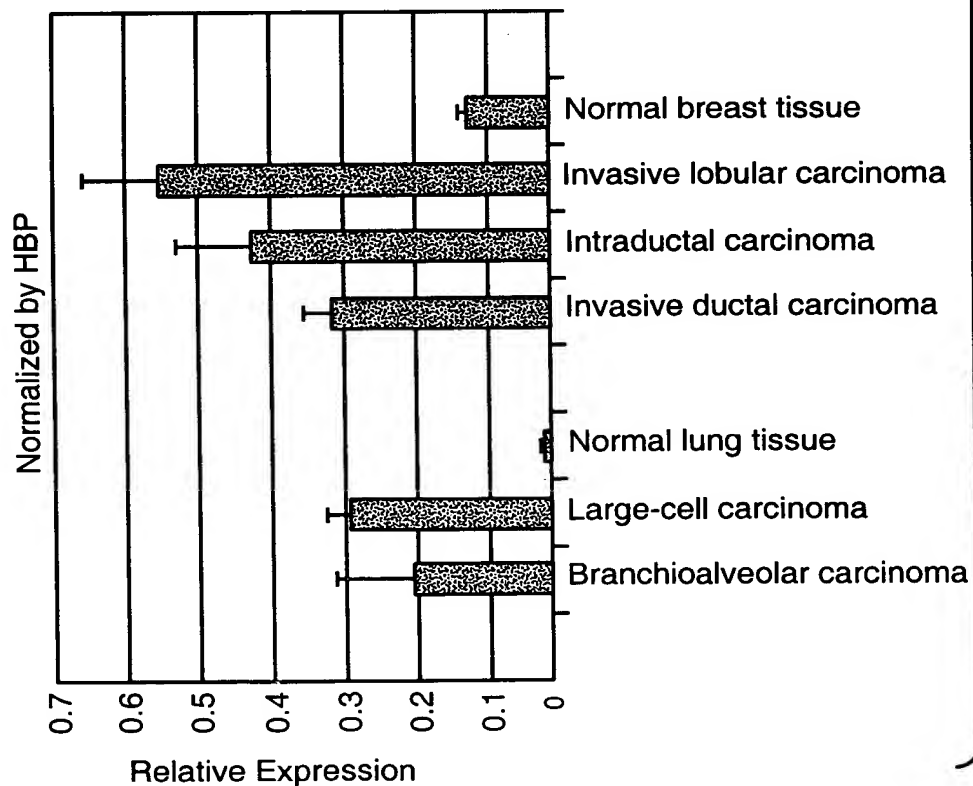
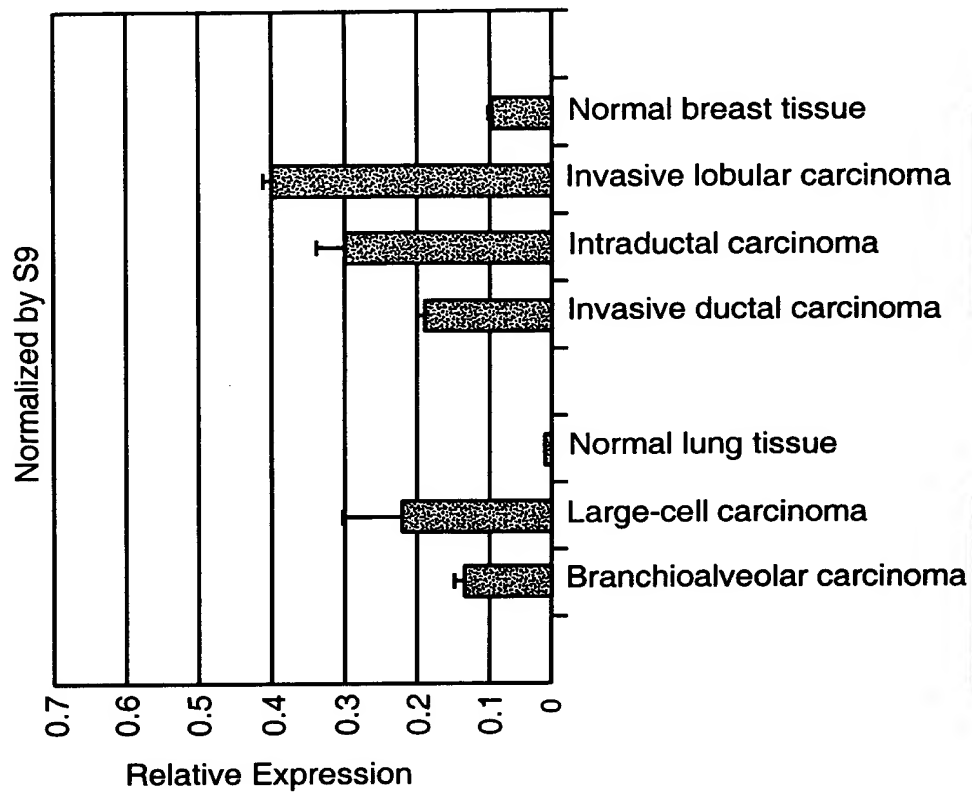
### Cell Cycle Analysis



**FIG. 10B**

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**mRNA Expression of Tankyrase Homologue in Several Tumors and Normal Tissues by a Taqman Analysis, mRNA Expression was Normalized by 90kDa Highly Basic Protein (HBP) and Ribosomal Protein S9 (S9)**

**FIG. 11**

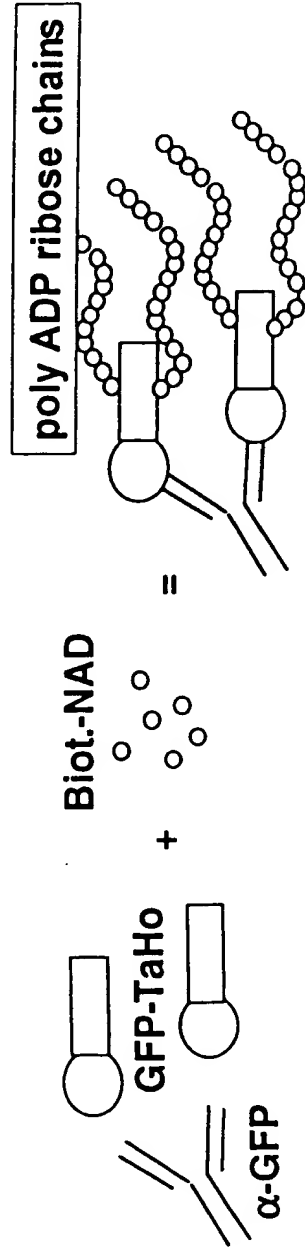
**Procedure for Nonisotopic Detection of Poly-ADP Ribosylation  
Using Anti-GFP mAb-Coated Plates**

Protein lysates from 293T cells normalized by GFP  
fluorescence and total protein

Immobilization of GFP-tankyrase homologue in anti-  
GFP Coated plates

Auto PARP reaction with Biotinylated-NAD in 96 wells

Detection of poly ADP ribose chains with Streptavidin-  
HRP and chemiluminescent substrate

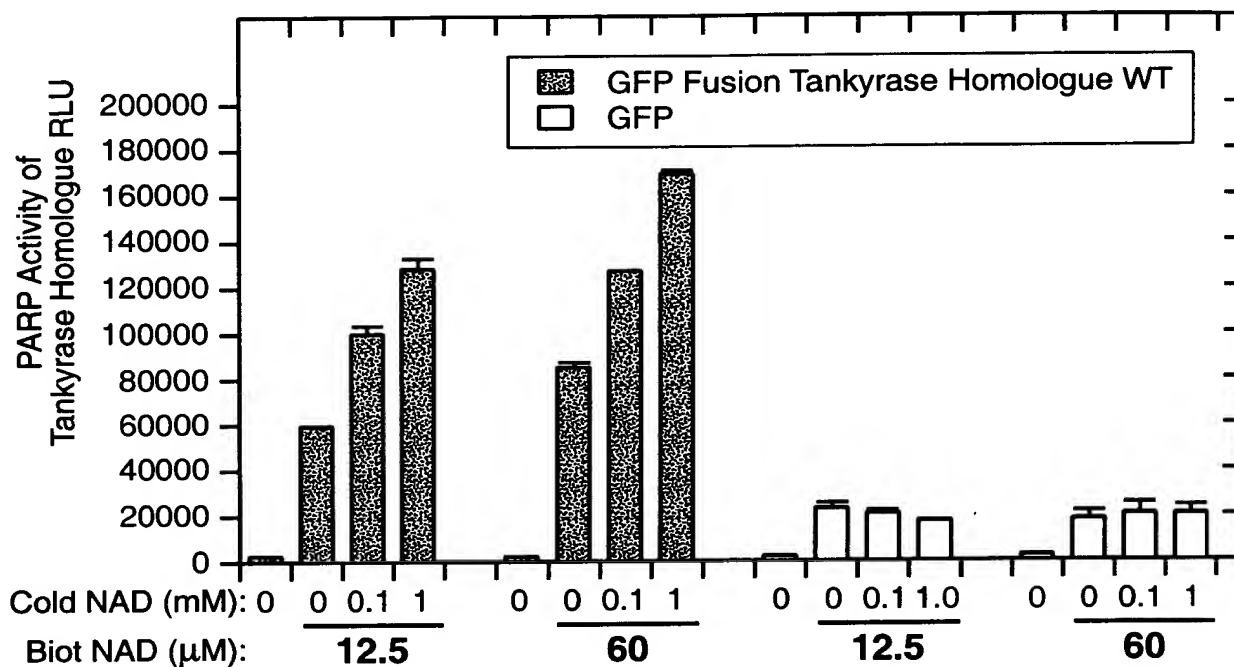


**FIG.\_12**



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### Non-Isotopic Plate-Based Detection of TaHo PARP Activity in the Presence of Biotinylated NAD

**FIG. 13**

### Comparison of IC<sub>50</sub> Values of the PARP Inhibitors

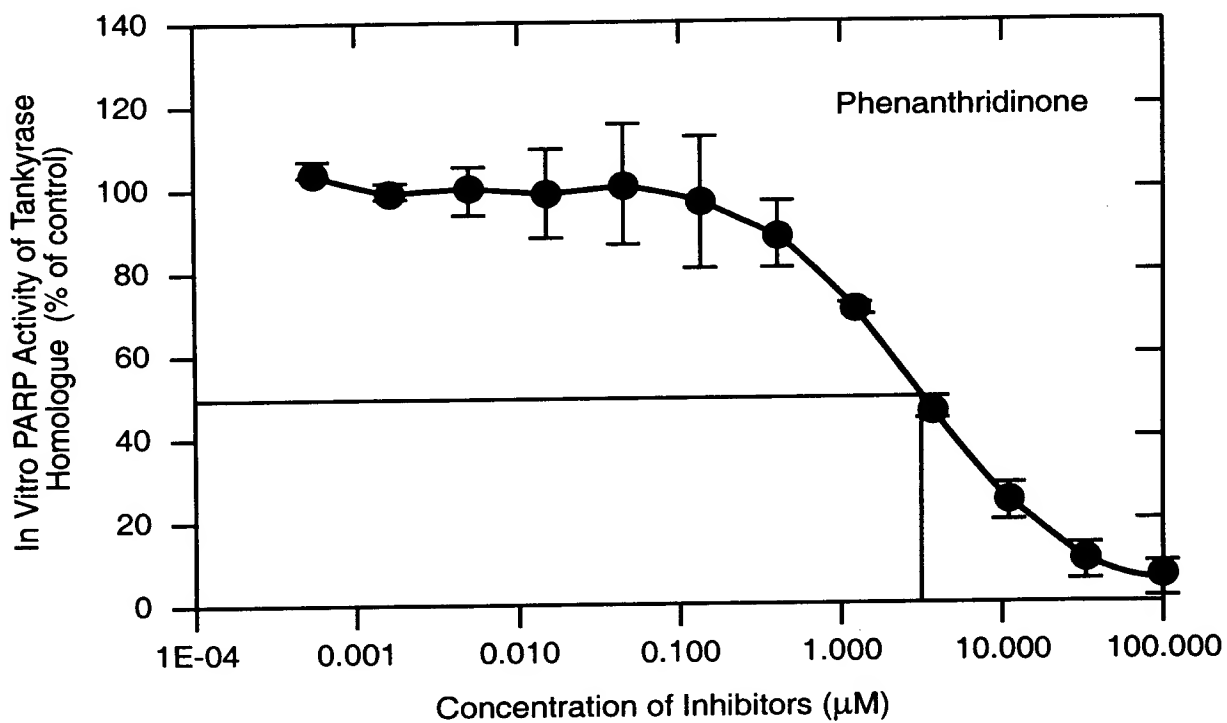
	Approximate IC <sub>50</sub> (nM)	hPARP assay IC <sub>50</sub> (nM)		
	TaHo	Rigel	Decker*	Rankin*
3AB	>50 000	5 000	2 000	5 400
6(5H)Phenanthridinone	1 000-2 000	300		
Niacinamide	>50 000	30 000	>>5 000	31 000

\* Decker P et al., Clinical Cancer Research. 1999 May; 5:1169-1172

\* Rankin PW et al., J Biol Chem. 1989 Mar 15;264(8):4312-4317

**FIG. 14**

### Inhibition of Tankyrase Homologue PARP Activity by hPARP Inhibitors

**FIG.\_15****FIG.\_16****FIG.\_16A****FIG.\_16B****FIG.\_16C**

**TH-1: Tankyrase Homologue isoform-1, TH-2: Tankyrase Homologue isoform-2**  
**M (Red): the first methionine in the sequence, Z: stop codon**  
**In this figure, the first methyonine in TH-1 sequence is position 1 (M1)**

Taho C terminus deletion mutant ends at position 429 (K) and adds 28 amino acids because of frame shift.

Tabo F/L mutant has the mutation at position 871

Taho E/A dc mutant has the mutation at position 948, ends at position 957 (A) and adds 2 amino acids.

TH-1  
TH-2  
-----  
RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQ -231

TH-1	-----
TH-2	AARLSASSPGGLALLAGPGLLLRLLALLLAVAAARIMSGRRRCAGGGAACASAAAEAVE -171

TH-1	-----*GGRKDVVEYLLQNGA	-111
TH-2	PAARELFEACRNGDVERVKRLVTPKVNSRDTAGRKSTPLHFAAGGGRKDVVEYLLQNGA	-111
	Ankyrin repeat	Ankyrin repeat

	TH-1	TH-2
SVQARDGGLIPLHNACSEFGHAEVNVLLLRHGADPNARDNWNYP	SVQARDGGLIPLHNACSEFGHAEVNVLLLRHGADPNARDNWNYP	SVQARDGGLIPLHNACSEFGHAEVNVLLLRHGADPNARDNWNYP
PLHEAAIKGKIDVCIV	PLHEAAIKGKIDVCIV	PLHEAAIKGKIDVCIV
-51	-51	-51

TH-1	TH-2
LLQHGAEPTIRNTDGR	LLQHGAEPTIRNTDGR
TALDLADPSAKAVLTGEYK	TALDLADPSAKAVLTGEYK
DELLESARSGNEEKMALLTPLNV	DELLESARSGNEEKMALLTPLNV
10	10

## FIG. 16B

	Ankyrin repeat	Ankyrin repeat
TH-1	NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVT	70
TH-2	NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVT	70
	Ankyrin repeat	Ankyrin repeat
TH-1	LVKHGACVNA MDLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSAIDLAPTQL	130
TH-2	LV	
	Ankyrin repeat	
TH-1	KERLAYEFKGHSLQLQAAREADVTRIKKHLSELMVNFKHPQTHETALHCAAASPYPKRKQI	190
	Ankyrin repeat	Ankyrin repeat
TH-1	CELLLRKGANINEKTEFLTPLHVASEKAHNDVVEVVVKHEAKVNALDNLGQTSLHRAAY	250
	Ankyrin repeat	
TH-1	CGHLQTCRLLLSYGCDPNIISLQGF TALQMGNE NVQQLQEGISLGNSEAD RQLLEA AKA	310
	Ankyrin repeat	Ankyrin repeat
TH-1	GDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHGADVHAKDKGGLVP	370
	Ankyrin repeat	Ankyrin repeat
TH-1	LHNACSYGHYEVAELLVKHGAVNVADLWKFTPLHEAAAKGYEICKLLQLQHGADPTKKN	430
	Ankyrin repeat	Ankyrin repeat
	GMEILLWILLKMEIQIFKICLGEMQLCZ	
TH-1	RDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKLSSPDNVNCRDTQGRHSTP	490
	Ankyrin repeat	

T

Deletion--

# FIG. 16C

TH-1	LHLAAGYNNLEVAEYLLQHGADVNAQDKGLIPLHNAASYGHVDVAALLIKYNACVNATD 550
	<div style="display: flex; justify-content: space-between;"> <div>Ankyrin repeat</div> <div>Ankyrin repeat</div> </div>
TH-1	KWAFTPLHEAAQKGRQTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPSPA 610
	<div style="display: flex; justify-content: space-between;"> <div>Ankyrin repeat</div> <div>Ankyrin repeat</div> </div>
TH-1	LPSCYKPQVLNGVRSPGATADALSSGPPSSLSAASSLDNLSGSFSELSSVSSSGTEG 670
	<div style="display: flex; justify-content: space-between;"> <div>Ankyrin repeat</div> <div>Ankyrin repeat</div> </div>
TH-1	ASSLEKKE--VPGVDFSITQFVRNLGLEHLMIDIFEREQITLDVLVEMGHKELKEIGINAY 730
	<div style="display: flex; justify-content: space-between;"> <div>SAM domain</div> <div></div> </div>
TH-1	GHRHKLIGVERLISGQQLNPYLTLNTSGSGTILIDLSPDDKEFQSVVEEMQSTVREHR 790
TH-1	DGGHAGGIFNRYNILKIQVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVNAIL 850
TH-1	HKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYIGGGTGPCVHKDRSCYICHRQLLFCR 910
	<div style="display: flex; justify-content: space-between;"> <div>• F→L mutation</div> <div>PARP domain</div> </div>
TH-1	VTLGKSFLQFSAMKMAHSPPGHSHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRP 970
	<div style="display: flex; justify-content: space-between;"> <div>•E→A</div> <div>•Deletion.</div> </div>
TH-1	EGMVDG 976

-----A-----LSZ